

### REMARKS

The undersigned attorney for Applicant wishes to thank Examiner Yu for the courtesy extended to her during a telephone interview on August 4, 2004. The undersigned attorney and the Examiner discussed the outstanding rejections under 35 U.S.C. §§ 112 and 102(e), and the proposed claim language as described herein. As indicated in Examiner Yu's Interview Summary dated August 11, 2004, the parties reached agreement on the proposed claim amendments, which will place the application in condition for allowance.

Claim 2, 4, 11-34, and 36 are currently pending. Claims 4 and 12 have been cancelled to expedite prosecution, and claims 5-10 and 17-34 have been cancelled in response to a restriction requirement. In addition, claim 2 has been amended. The amendment to claim 2 finds support in the specification and is discussed in the relevant sections below. No new matter is added. Applicant reserves the right to prosecute the subject matter of the cancelled claims in subsequent continuing and/or divisional applications. Following entry of this amendment, claim 2, 11, 13-15, and 36 will be pending.

#### The Objection of Claim 4 under 35 U.S.C. § 1.75(c)

Claim 4 was objected to as being improper for failing to further limit the subject matter of claim 2. Applicant has cancelled claim 4 thereby obviating the objection.

#### The Rejection under 35 U.S.C. §112, First Paragraph

Claims 2, 4, and 11-16 remain rejected for lack of written description under 35 U.S.C. §112, first paragraph. The Office Action states that the claims are drawn to a genus of proteins comprising residues 168-175 of SEQ ID NO:2, wherein the protein has anti-angiogenic activity. The Office Action alleges that the specification does not provide adequate written description for claim 2 as written because the specification discloses only one protein sequence comprising the common structural feature, i.e., the mouse endostatin sequence comprising amino acid residues 168-175 of SEQ ID NO:2.

Although not acquiescing to the rejection, Applicant has cancelled claims 4, 12 and 16, and amended claim 2, from which claims 11 and 13-15 depend, for the sole purpose of

expediting the prosecution of the present application. As indicated in the Examiner's Interview Summary, Examiner Yu has agreed that the cancellation of claims 4 and 12 (and 16 by implication), and amendment of claim 2 to recite an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the polypeptide *does not* contain the amino acid sequence of SEQ ID NO:25 (i.e., the nine C'-terminal amino acids of SEQ ID NO:2), will obviate this rejection. As discussed more fully below, Applicant has amended claim 2 and cancelled claims 4, 12 and 16, and respectfully requests the withdrawal of this rejection.

As amended, claim 2 (and its dependent claims 11, 13-15) recite an isolated anti-angiogenic polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the isolated polypeptide *does not* contain the amino acid sequence of SEQ ID NO:25. Examiner Yu has agreed that claim 2, if amended to specifically exclude the amino acid sequence of SEQ ID NO:25, is fully supported by the specification and satisfies the written description requirement of 35 U.S.C. § 112, first paragraph. As amended, claim 2 recites an exemplified polypeptide (i.e., having the amino acid sequence of SEQ ID NO:2 minus 9 C'-terminal residues), and therefore is no longer directed to a "genus of proteins" comprising residues 168-175 of SEQ ID NO:2.

Support for this amendment is found in Figure 2 of the present application and page 4, line 19, which describes the sequence of an isolated polypeptide EM1, which comprises the amino acid sequence of SEQ ID NO:2 but excludes the nine consecutive amino acids from the C-terminus of said SEQ ID NO:2. In addition, Example 12 (page 58) provides further detailed descriptions of two closely related C-terminus mutants and the *in vivo* anti-angiogenic activity in an RCC tumor model.

In view of the above, the specification provides sufficient written description for the claimed isolated polypeptide, namely an anti-angiogenic polypeptide comprising the amino acid sequence of SEQ ID NO:2, but which does not contain the amino acid sequence set forth in SEQ ID NO:25 (i.e., the nine consecutive amino acids from the C-terminus of said SEQ ID NO:2). Because claim 2 as amended is deemed allowable (as indicated in the Interview Summary), claims 11 and 13-15, which depend therefrom, are also allowable. Applicant respectfully requests the withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

The Rejection under 35 U.S.C. §112, Second Paragraph

Claims 2, 4, and 11-16 were rejected under 35 U.S.C. §112, second paragraph, for indefiniteness. The Office Action states that claim 2 is confusing because the transitional phrase “comprises” can be interpreted as encompassing everything that comes after the transitional phrase (including the last 9 amino acids at the C-terminus of SEQ ID NO:2) or, alternatively, as a deletion mutant comprising 168-175 of SEQ ID NO:2 but excluding the last 9 C'-terminal amino acids of SEQ ID NO:2.

As discussed above, claim 2 (and hence claims 11-16 which depend therefrom) has been amended to recite an isolated anti-angiogenic polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the isolated polypeptide *does not* contain the amino acid sequence of SEQ ID NO:25. Amended claim 2 particularly points out and distinctly claims the subject matter which applicant regards as one aspect of the invention, i.e., an isolated polypeptide having anti-angiogenic activity, which has the amino acid sequence set forth in SEQ ID NO:2, minus the nine C'-terminal residues. Examiner Yu has agreed that claim 2 as amended is clear and definite, and thus satisfies the requirements of 35 U.S.C. § 112, second paragraph. Because claim 2 as amended is deemed allowable, claims 11 and 13-15, which depend therefrom, are also allowable. Applicant respectfully requests the withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

The Rejection under 35 U.S.C. §102(e)

Claims 2, 4, and 11-16 are rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,080,728 (“the ‘728 patent”). Specifically, the Office Action states, in the paragraph bridging pages 5 and 6, that columns 7-8 and 49-50 of the ‘728 patent teaches a polypeptide as recited in pending claim 2. According to the Office Action, an “attached sequence alignment” shows that “SEQ ID NO:36 of the prior art comprises amino acid residues 168-175 of SEQ ID NO:2 but does not contain instant SEQ ID NO:25.” The Office Action further states that the ‘728 patent teaches pharmaceutically compatible carrier, and thus anticipates claims 2, 4, and 11-16 of the present invention.

Although not acquiescing to this rejection, Applicant has amended claim 2 to recite an isolated anti-angiogenic polypeptide comprising the amino acid sequence of SEQ ID NO:2, wherein the isolated polypeptide does not contain the amino acid sequence of SEQ ID NO:25. The polypeptide described in the '728 patent, which has the amino acid sequence of SEQ ID NO:36, does not comprise the amino acid sequence of SEQ ID NO:2 as required by amended claim 2, and thus does not anticipate the claimed invention. For example, the polypeptide identified in SEQ ID NO:36 of the '728 patent does not comprise amino acids 35-40 of SEQ ID NO: 2, and thus does not anticipate amended claim 2. Because claim 2 as amended is deemed allowable, claims 11 and 13-15, which depend therefrom, are also allowable. Applicant respectfully requests the withdrawal of the rejection of claims 2, 11, and 13-15 under 35 U.S.C. §102(e).

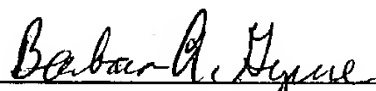
#### CONCLUSION

Claims 5-10 and 17-34, directed to a non-elected invention, have been cancelled and will be pursued in a divisional application. Claims 4, 12 and 16 have also been cancelled. Claim 2 has been amended to obviate all outstanding rejections. As the result of this amendment, claims 2, 11, 13-15, and 36 are currently pending.

Applicants submit that in view of the foregoing remarks, all issues relevant to patentability raised in the Office Action have been addressed. Applicants respectfully request the withdrawal of rejections over the claims of the present invention.

Respectfully submitted,

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